Amendments to the Specification:

At the end of the application, please replace the current Sequence Listing with the attached Sequence Listing.

Please replace the paragraph beginning on page 2, line 26, with the following rewritten paragraph:

In this respect, the invention relates to an in vitro method for the diagnosis/prognosis of thrombosis, comprising the following steps:

A – the nucleic material is extracted from a biological sample,

B – at least one pair of amplification primers is used to obtain amplicons of at least one target sequence of the nucleic material,

C – at least one detection probe is used to detect the presence of said amplicons, characterized in that, in step B, said pair of primers comprises at least one amplification primer comprising at least 10 nucleotide units of a nucleotide sequence chosen from SEQ ID ~~Nos. 1; 3 to 8, 15 and 16~~NO: 1, 2, 3, 4, 5, 6, 7, 8, 15 or 16.

Please replace the paragraph beginning on page 5, line 16, with the following rewritten paragraph:

For the purpose of the present invention, the term "amplification primer" is intended to mean a nucleic sequence comprising from 10 to 100 nucleotide units, preferably from 15 to 25 nucleotide units. This amplification primer comprises at least 10, preferably 15, and even more preferably 20, nucleotide units of a sequence chosen from SEQ ID ~~Nos. 1; 3 to 8~~NO: 1, 2, 3, 4, 5, 6, 7, 8, 15 or 16.

Please replace the paragraph beginning on page 5, line 21, with the following rewritten paragraph:

For the purpose of the present invention, an amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of

- a sequence homologous to SEQ ID ~~Nos. 1; 3 to SEQ ID Nos. 8; 15 and 16~~NO: 1, 2, 3, 4, 5, 6, 7, 8, 15 or 16, i.e.
    - the sequence complementary to SEQ ID ~~Nos. 1; 3 to 8; 15 and 16~~NO: 1, 2, 3, 4, 5, 6, 7, 8, 15 or 16,
    - a sequence exhibiting sufficient homology to hybridize to SEQ ID ~~Nos. 1; 3 to SEQ ID Nos. 8; 15 and 16~~NO: 1, 2, 3, 4, 5, 6, 7, 8, 15 or 16 or to the sequence complementary to SEQ ID ~~Nos. 1; 3 to SEQ ID Nos. 8; 15 and 16~~ NO: 1, 2, 3, 4, 5, 6, 7, 8, 15 or 16,
- a sequence comprising a sequence of SEQ ID ~~Nos. 1; 3 to SEQ ID Nos. 8; 15 and 16~~ NO: 1, 2, 3, 4, 5, 6, 7, 8, 15 or 16 (or a sequence homologous to SEQ ID ~~Nos. 1; 3 to SEQ ID Nos. 8; 15 and 16~~ NO: 1, 2, 3, 4, 5, 6, 7, 8, 15 or 16, as defined above) in which the ~~uracil~~ thymine bases are substituted with ~~thymine~~uracil bases, and which would have the same function as the amplification primer according to the invention, i.e. that amplifying all or part of the gene coding factor V (SEQ ID ~~Nos. 1; 3 to 4~~NOS: 1-4) that may contain the Leiden mutation or all or part of the gene encoding factor II (SEQ ID ~~Nos.~~ NOS: 5~~ to 8~~, 15 and 16), that may contain the 20210 mutation, is considered to be equivalent to the amplification primer according to the invention.

Please replace the paragraph beginning on page 9, line 12, with the following rewritten paragraph:

According to a preferred embodiment of the invention, during step C), said detection probe comprises at least 10, preferably 15, ~~and even more preferably 20,~~ nucleotide units of a nucleotide sequence chosen from SEQ ID ~~Nos. 9 to 12; 17 and 18~~NO: 9, 10, 11, 12, 17 or 18. Thus, the use of a detection probe comprising SEQ ID ~~No.~~NO: 9 makes it possible to diagnose the ~~presence~~absence of the factor V Leiden mutation, whereas the use of a detection probe comprising SEQ ID ~~No.~~NO: 10 makes it possible to diagnose the ~~absence~~presence of the factor V Leiden mutation.

Please replace the paragraph beginning on page 9, line 19, with the following rewritten paragraph:

Similarly, the use of a detection probe comprising SEQ ID ~~No.~~NO: 11 makes it possible to detect the presence of the factor II 20210 mutation, whereas the use of a detection probe comprising SEQ ID ~~No.~~NO: 12 makes it possible to detect the absence of the factor II 20210 mutation. Furthermore, the use of a detection probe comprising SEQ ID ~~No.~~NO: 17 makes it possible to detect the presence of the factor II 20210 mutation, whereas the use of a detection probe comprising SEQ ID ~~No.~~NO: 18 makes it possible to detect the absence of the factor II 20210 mutation.

Please replace the paragraph beginning on page 9, line 26, with the following rewritten paragraph:

According to a preferred embodiment of the invention, during step B, said pair of primers is chosen from the following pairs of primers:

- a first amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 1 and a second amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 2; by way of indication, when the first primer has the sequence SEQ ID ~~No.~~NO: 1, and the second primer has the sequence SEQ ID ~~No.~~NO: 2, an amplicon, specific for the gene encoding factor V, 159 base pairs in size, which corresponds to the sequence 36568-36726 on a sequence of the reference gene encoding the factor V (NT_004668), is obtained. This amplicon can contain the mutated allele responsible for the Leiden mutation or the wild-type allele, the allele being characterized during step C;
- a first amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 3 and a second amplification primer comprising at least 10, preferably 15, and even more preferably 20 nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 4; by way of indication, when the first primer has the sequence SEQ ID ~~No.~~NO: 3, and the second primer has the sequence SEQ ID ~~No.~~NO: 4, an amplicon, specific for the gene encoding factor V, 374 base pairs in size, which corresponds to the sequence 36568-36941 on the sequence of the reference gene encoding factor V (NT_004668),

is obtained. This amplicon can contain the mutated allele responsible for the Leiden mutation or the wild-type allele, the allele being characterized during step C;

- a first amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 5 and a second amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 6; by way of indication, when the first primer has the sequence SEQ ID ~~No.~~NO: 5, and the second primer has the sequence SEQ ID ~~No.~~NO: 6, an amplicon, specific for the gene encoding factor II, 145 base pairs in size, which corresponds to the sequence 21455-21599 on the sequence of the reference gene encoding factor II (AF478696), is obtained. This amplicon can contain the mutated allele responsible for the factor II 20210 mutation or the wild-type allele, the allele being characterized during step C;
- a first amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 7, and a second amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 8; by way of indication, when the first primer has the sequence SEQ ID ~~No.~~NO: 7, and the second primer has the sequence SEQ ID ~~No.~~NO: 8, an amplicon, specific for the gene encoding factor II, 434 base pairs in size, which corresponds to the sequence 21217-21650 on the sequence of the reference gene encoding factor II (AF478696), is obtained. This amplicon can contain the mutated allele responsible for the factor II 20210 mutation or the wild-type allele, the allele being characterized during step C;
- a first amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 15 and a second amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 16; by way of indication, when the first primer has the sequence SEQ ID ~~No.~~NO: 15, and the second primer has the sequence SEQ ID ~~No.~~NO: 16, an amplicon, specific for the gene encoding factor II, ~~108~~109 base pairs in size, which corresponds to the sequence 21465-21573 on the sequence of the reference gene encoding factor II (AF478696), is obtained. This amplicon can contain the mutated allele responsible for the factor II 20210 mutation, or the wild-type allele, the allele being characterized during step C.

Please replace the paragraph beginning on page 11, line 19, with the following rewritten paragraph:

According to a preferred embodiment of the invention, said pair of primers comprises at least one amplification primer comprising a promoter allowing the initiation of transcription by a T7 bacteriophage polymerase. Preferably, this first amplification primer comprises a sequence chosen from the sequences SEQ ID ~~Nos.~~NO: 13 ~~to~~or 14.

Please replace the paragraph beginning on page 12, line 16, with the following rewritten paragraph:

The present invention also relates to an amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of a nucleotide sequence chosen from SEQ ID ~~Nos. 1; 3 to 8; 15 and 16~~NO: 1, 2, 3, 4, 5, 6, 7, 8, 15 or 16.

Please replace the paragraph beginning on page 12, line 19, with the following rewritten paragraph:

According to a preferred embodiment of the invention, the amplification primer comprises a promoter allowing the initiation of transcription by a T7 bacteriophage polymerase. Preferably, such an amplification primer comprises a sequence chosen from the sequences SEQ ID ~~Nos.~~NO: 13 ~~to~~or 14.

Please replace the paragraph beginning on page 12, line 23, with the following rewritten paragraph:

The invention also relates to a pair of amplification primers chosen from the following pairs of primers:

- a first amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 1 and a second amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 2; by way of indication, when the first primer has the sequence SEQ ID ~~No.~~NO: 1, and the second primer has the sequence SEQ ID ~~No.~~NO: 2, an amplicon, specific for the gene

encoding factor V, 159 base pairs in size, which corresponds to the sequence 36568-36726 on a sequence of the reference gene encoding the factor V (NT_004668), is obtained;

- a first amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 3 and a second amplification primer comprising at least 10, preferably 15, and even more preferably 20 nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 4; by way of indication, when the first primer has the sequence SEQ ID ~~No.~~NO: 3, and the second primer has the sequence SEQ ID ~~No.~~NO: 4, an amplicon, specific for the gene encoding factor V, 374 base pairs in size, which corresponds to the sequence 36568-36941 on the sequence of the reference gene encoding factor V (NT_004668), is obtained;
- a first amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 5 and a second amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 6; by way of indication, when the first primer has the sequence SEQ ID ~~No.~~NO: 5, and the second primer has the sequence SEQ ID ~~No.~~NO: 6, an amplicon, specific for the gene encoding factor II, 145 base pairs in size, which corresponds to the sequence 21455-21599 on the sequence of the reference gene encoding factor II (AF478696), is obtained;
- a first amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 7, and a second amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 8; by way of indication, when the first primer has the sequence SEQ ID ~~No.~~NO: 7, and the second primer has the sequence SEQ ID ~~No.~~NO: 8, an amplicon, specific for the gene encoding factor II, 434 base pairs in size, which corresponds to the sequence 21217-21650 on the sequence encoding the reference gene encoding factor II (AF478696), is obtained;
- a first amplification primer comprising at least 10, preferably 15, and even more preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 15 and a second amplification primer comprising at least 10, preferably 15, and even more

preferably 20, nucleotide units of the nucleotide sequence SEQ ID ~~No.~~NO: 16; by way of indication, when the first primer has the sequence SEQ ID ~~No.~~NO: 15, and the second primer has the sequence SEQ ID ~~No.~~NO: 16, an amplicon, specific for the gene encoding factor II, ~~108~~109 base pairs in size, which corresponds to the sequence 21465-21573 on the sequence of the reference gene encoding factor II (AF478696), is obtained.

Please replace the paragraph beginning on page 14, line 7, with the following rewritten paragraph:

According to a preferred embodiment of the invention, said first primer comprises a promoter allowing the initiation of transcription by a T7 bacteriophage polymerase. Preferably, this first amplification primer comprises a sequence chosen from the sequences SEQ ID ~~Nos.~~NO: 13 ~~to~~or 14.

Please replace the paragraph beginning on page 14, line 20, with the following rewritten paragraph:

Figures 1 and 2 represent the genotyping of various cell lines for the factor V mutation + 1691 G/A, by virtue of the simultaneous presence of the molecular beacons of SEQ ID ~~No.~~NO: 10 and SEQ ID ~~No.~~NO: 9 in the reaction mixture.

Please replace the paragraph beginning on page 14, line 23, with the following rewritten paragraph:

Thus, Figure 1a represents the genotyping of the GM16000C cell line homozygous for the factor V wild-type allele (+1691-G), while Figure 1b represents the genotyping of the GM14899 cell line homozygous for the factor V mutated allele (+1691-A). The white squares represent the detection of the fluorescence of the "molecular beacons" of SEQ ID ~~No.~~NO: 9, making it possible to reveal the factor V wild-type allele, while the black triangles represent the detection of the fluorescence of the "molecular beacons" of SEQ ID ~~No.~~NO: 10, allowing the detection of the mutated allele (Leiden mutation).

Please replace the paragraph beginning on page 14, line 30, with the following rewritten paragraph:

Figure 2 represents the genotyping of the GM16028B cell line heterozygous for the factor V +1691 mutation. The white squares represent the detection of the fluorescence of the "molecular beacons" of SEQ ID ~~No.~~NO: 9, making it possible to reveal the factor V wild-type allele, while the black triangles represent the detection of the fluorescence of the "molecular beacons" of SEQ ID ~~No.~~NO: 10, allowing the detection of the mutated allele (Leiden mutation).

Please replace the paragraph beginning on page 15, line 4, with the following rewritten paragraph:

Figures 3 and 4 represent the genotyping of various cell lines for the factor II mutation +20210 G/A, by virtue of the simultaneous presence of the molecular beacons OGH 916 (SEQ ID ~~No.~~NO: 11, +20210-A) and OGH 1104 (SEQ ID ~~No.~~NO: 12, ~~+2010-G~~+20210-G) in the reaction mixture.

Please replace the paragraph beginning on page 15, line 8, with the following rewritten paragraph:

In this respect, Figure 3a represents the genotyping of the GM14899 cell line homozygous for the factor II wild-type allele (+20210-G), while Figure 3b represents the genotyping of the GM16000C cell line homozygous for the factor II mutated allele (+20210-A). The crosses represent the detection of the "molecular beacons" of SEQ ID ~~No.~~NO: 12, making it possible to reveal the wild-type allele, while the circles represent the detection of the "molecular beacons" of SEQ ID ~~No.~~NO: 11, allowing the detection of the factor II 20210 mutation.

Please replace the paragraph beginning on page 15, line 15, with the following rewritten paragraph:

Figure 4 represents the genotyping of the GM16028B cell line heterozygous for the factor II +20210 mutation. The presence of the mutated allele (black circles) and of the wild-type allele (curved with crosses) is clearly detected. The crosses represent the detection of the

"molecular beacons" of SEQ ID ~~No.~~NO: 12, making it possible to reveal the wild-type allele, while the circles represent the detection of the "molecular beacons" of SEQ ID ~~No.~~NO: 11, allowing the detection of the factor II 20210 mutation.

Please replace the paragraph beginning on page 15, line 21, with the following rewritten paragraph:

Figures 5 and 6 represent the genotyping of various cell lines (~~GM 14899~~GM14899: A/A; ~~GM 16028B~~GM16028B: A/G; ~~GM 16000C~~GM16000C: G/G) for the factor V +1691 mutation, by virtue of the presence of the molecular beacons SEQ ID ~~Nos.~~NOS: 3 and 4 in the reaction mixture.

Please replace the paragraph beginning on page 15, line 28, with the following rewritten paragraph:

Thus, Figure 6 represents the detection of the ROX beacon specific for the G allele of factor V (G+1691A) using DNA from the GM14899 line: A/A (homozygous, mutated allele; triangles); GM16028B line (A/G heterozygous; crosses) and ~~GM 16000C~~GM16000C line (G/G homozygous, wild-type allele, circles).

Please replace the paragraph beginning on page 16, line 1, with the following rewritten paragraph:

Figures 7 and 8 represent the genotyping of various cell lines (~~GM 14899~~GM14899: G/G; ~~GM 16028B~~GM16028B: A/G; ~~GM 16000C~~GM16000C: A/A) for the factor II +20210 mutation, by virtue of the presence of the molecular beacons SEQ ID ~~Nos.~~NOS: 7 and 8 in the reaction mixture.

Please replace the paragraph beginning on page 16, line 4, with the following rewritten paragraph:

Thus, Figure 7 represents the detection of the FAM beacon specific for the G allele of factor II (G+20210A) using DNA from the GM14899 line: G/G (homozygous, mutated allele;

triangles); GM16028B line (A/G heterozygous; crosses) and ~~GM 16000C~~GM16000C line (A/A homozygous, wild-type allele, circles).

Please replace the paragraph beginning on page 16, line 8, with the following rewritten paragraph:

Thus, Figure 8 represents the detection of the ROX beacons specific for the A allele of factor II (G+20210A) using DNA from the GM14899 line: G/G (homozygous, mutated allele; triangles); GM16028B line (A/G heterozygous; crosses) and ~~GM 16000C~~GM16000C line (A/A homozygous, wild-type allele, circles).

Please replace the paragraph beginning on page 16, line 24, with the following rewritten paragraph:

Cell lines – Three lymphoblastoid cell lines of known genotype for the factor V Leiden ~~mutations~~mutation and the factor II 20210 mutation (Coriell cell repository) were used: The GM14899 line expresses only the factor V Leiden mutation: this line is homozygous for the factor V Leiden mutation (A/A) and homozygous for the wild-type allele at position ~~20120~~20210 of factor II (G/G). The GM16000C line expresses only the factor II 20210 mutation: this line is homozygous for the factor II 20210 mutation (A/A) and homozygous for the wild-type allele at position 1691 of factor V (G/G). The GM16028B line is heterozygous for the 2 mutations (G/A).

Please replace the paragraph beginning on page 17, line 14, with the following rewritten paragraph:

Cloning of the region of interest: In order to obtain a large amount of DNA of the region that may express the factor V Leiden mutation, a PCR was carried out using the genomic DNA as obtained above, from cell lines or blood samples, using a pair of amplification primers comprising SEQ ID ~~No.~~NO: ~~3,~~ (5' AGTGCTTAACAAGACCATACTA 3') for the first primer, and SEQ ID ~~No.~~NO: ~~4,~~ (5' AACAGACCTGGAATTTGAAACTAA 3') for the second primer. The parameters of the PCR were as follows: 2 min at 95°C; 30 cycles of 30 s at 95°C, 30 s at 55°C, 30 s at 72°C; followed by 7 min at 72°C. The amplicons thus obtained

were cloned into a vector PCR-Trap (GeneHunter, USA) and verified by sequencing. The plasmids, containing either a nucleotide G or a nucleotide A at position 1691, were amplified and purified using a Plasmid Maxi kit (Qiagen; Germany).

Please replace the paragraph beginning on page 17, line 25, with the following rewritten paragraph:

In order to obtain a large amount of DNA of the region that may express the factor II 20210 mutation, a PCR was carried out using the genomic DNA as obtained above, from cell lines or from blood samples, using a pair of amplification primers comprising SEQ ID ~~No.~~NO: 7, (5' TCTAGAAACAGTTGCCTGGC 3') for the first primer, and SEQ ID ~~No.~~NO: 8, (5' CTACCAGCGTGCCACCAGGT 3') for the second primer. The parameters of the PCR were as follows: 2 min at 95°C; 30 cycles of 30 s at 95°C, 30 s at 55°C, 30 s at 72°C; followed by 7 min at 72°C. The amplicons thus obtained were cloned into a vector PCR-Trap (GeneHunter, USA) and verified by sequencing. The plasmids, containing either a nucleotide G or a nucleotide A at position 1691, were amplified and purified using a Plasmid Maxi kit (Qiagen; Germany).

Please replace the paragraph beginning on page 18, line 11, with the following rewritten paragraph:

Thus, the reaction medium for detecting the presence of the factor V Leiden mutation comprised:

- 0.2 µM (final concentration) of a first amplification primer of SEQ ID ~~No.~~NO: 2, (5' AGT GCT TAA CAA GAC CAT ACT A 3'),
- 0.2 µM (final concentration) of a second amplification primer of SEQ ID ~~No.~~NO: 1, (5' AAA TTC TCA GAA TTT CTG AAA GG 3') comprising the T7 phage polymerase promoter, i.e. an amplification primer whose complete sequence corresponds to SEQ ID ~~No.~~NO: 13, (5' aat tct aat acg act cac tat agg gag aAA ATT CTC AGA ATT TCT GAA AGG 3'),
- 0.2 µM (final concentration) of "molecular beacons" of SEQ ID ~~No.~~NO: 9, (5' CTG GAC AGG CGA IGA A 3'), labeled with a ROX (6-carboxy-X-rhodamine) fluorophore in the 5' position, and of a "quencher" (Dabsyl) in the 3'

position (complete sequence: 5' ROX-*cgatcg* CTGGACAGGCGAIGAA*cgatcg*-Dabsyl 3' (SEQ ID NO: 20)). This "molecular beacon" made it possible to reveal the absence of the Leiden mutation,

- 0. 1 µM (final concentration) of "molecular beacons" of SEQ ID ~~No.~~NO: 10, (3' CTG GAC AGG CAA IGA A 3'), labeled with a FAM (6-carboxyfluorescein) fluorophore in the 5' position, and of a "quencher" (Dabsyl) in the 3' position (complete sequence: 5' FAM-*cgatcg* CTGGACAGGCAAIGAA*cgatcg*-Dabsyl 3' (SEQ ID NO: 21)). This "molecular beacon" made it possible to reveal the presence of the Leiden mutation.

Please replace the paragraph beginning on page 19, line 1, with the following rewritten paragraph:

For factor II, the following were added to the reaction medium:

- 0.2 µM (final concentration) of a first amplification primer of SEQ ID ~~No.~~NO: 6, (5' TTC TGG GCT CCT GGA ACC AA 3'),
- 0.2 µM (final concentration) of a second amplification primer of SEQ ID ~~No.~~NO: 5, (5' ATT ACT GGC TCT TCC TGA GC 3'), comprising the T7 phage polymerase promoter, i.e. an amplification primer whose complete sequence corresponds to SEQ ID ~~No.~~NO: 14,
- 0.1 µM (final concentration) of "molecular beacons" of SEQ ID ~~No.~~NO: 11, (5' ACT CTC AGC AAG CCT CAA 3'), labeled with a ROX (6-carboxy-X-rhodamine) fluorophore in the 5' position and of a "quencher" (Dabsyl) in the 3' position (complete sequence: 5' ROX-cga tcg ACT CTC AGC AAG CCT CAA cga tcg-Dabsyl 3' (SEQ ID NO: 22)). This "molecular beacon" made it possible to reveal the presence of the factor II 20210 mutation,
- 0.2 µM (final concentration) of "molecular beacons" of SEQ ID ~~No.~~NO: 12, (5' ACT CTC AGC GAG ICT CAA 3'), labeled with a FAM (6-carboxyfluorescein) fluorophore in the 5' position, and of a "quencher" (Dabsyl) in the 3' position (complete sequence: 5' FAM-cgg tcg ACT CTC AGC GAG ICT CAA cga ccg-Dabsyl 3' (SEQ ID NO: 23)). This "molecular beacon" made it possible to reveal the absence of the factor II 20210 mutation.

Please replace the paragraph beginning on page 19, line 20, with the following rewritten paragraph:

As shown in Figure 1, the "molecular beacon" of SEQ ID ~~No.~~NO: 9, labeled with a ROX (6-carboxy-X-rhodamine) fluorophore is very specific for the wild-type allele: in fact, the fluorescence was exponential, before the appearance of a plateau, when the reaction was carried out using a cell line not expressing the Leiden mutation (curve of white squares; Figure 1a), whereas the fluorescence remained baseline when the reaction was carried out using a cell line expressing the Leiden mutation (curve of white squares: Figure 1b).

Please replace the paragraph beginning on page 19, line 20, with the following rewritten paragraph:

The "molecular ~~beacons~~"beacon" of SEQ ID ~~No.~~NO: 10, labeled with a FAM (6-carboxyfluorescein) fluorophore is specific with the mutated allele. In fact, the fluorescence was exponential when the reaction was carried out using a cell line expressing the Leiden mutation (curve of triangles; Figure 1b), while the fluorescence remained baseline when the reaction was carried out using a cell line not expressing the Leiden mutation (curve of triangles; Figure 1a).

Please replace the paragraph beginning on page 20, line 1, with the following rewritten paragraph:

By using 2 different fluorophores, the "molecular beacon" of SEQ ID ~~No.~~NO: 9 could be used simultaneously with a "molecular beacon" of SEQ ID ~~No.~~NO: 10, which made it possible to very rapidly detect, using a single reaction, the presence or absence of the factor V Leiden mutation. The results are given in Figure 2, obtained from a cell line heterozygous for the factor V Leiden mutation.

Please replace the paragraph beginning on page 20, line 6, with the following rewritten paragraph:

These two "molecular beacons", used simultaneously with the amplification primers of SEQ ID ~~No.~~NO: 1 and SEQ ID ~~No.~~NO: 2 therefore make it possible to differentiate clearly between the two alleles.

Please replace the paragraph beginning on page 20, line 21, with the following rewritten paragraph:

These results demonstrate that the use of a "molecular beacon" of SEQ ID ~~No.~~NO: 9 simultaneously with the NASBA amplification with a pair of amplification primers, comprising a first primer comprising SEQ ID ~~No.~~NO: 1 and a second primer comprising SEQ ID ~~No.~~NO: 2, made it possible to detect very specifically the absence of the Leiden mutation. The use of a "molecular beacon" of SEQ ID ~~No.~~NO: 10 simultaneously with NASBA amplification with a pair of amplification primers, comprising a first primer comprising SEQ ID ~~No.~~NO: 1 and a second primer comprising SEQ ID ~~No.~~NO: 2, made it possible to detect very specifically the presence of the Leiden mutation.

Please replace the paragraph beginning on page 21, line 1, with the following rewritten paragraph:

As shown in Figure 3, the "molecular beacon" of SEQ ID ~~No.~~NO: 12, labeled with a FAM (6-carboxyfluorescein) fluorophore is very specific for the factor II wild-type allele. In fact, the fluorescence was exponential, when the reaction was carried out using a cell line not expressing the 20210 mutation (curve of crosses; Figure 3a), while the fluorescence remained baseline when the reaction was carried out using a cell line expressing this mutation (curve of crosses; Figure 3b).

Please replace the paragraph beginning on page 21, line 8, with the following rewritten paragraph:

The "molecular ~~beacons~~"beacon" of SEQ ID ~~No.~~NO: 11, labeled with a ROX (6-carboxy-X-rhodamine) fluorophore is specific for the mutated allele. The fluorescence was exponential, when the reaction was carried out using a cell line expressing the 20210 mutation (curve of

circles; Figure 3b), while the fluorescence remained baseline when the reaction was carried out using a cell line not expressing this mutation (curve of circles; Figure 3a).

Please replace the paragraph beginning on page 21, line 14, with the following rewritten paragraph:

By using 2 different fluorophores, the "molecular beacon" of SEQ ID ~~No.~~NO: 11 could be used simultaneously with a "molecular beacon" of SEQ ID ~~No.~~NO: 12, which made it possible to very rapidly detect, using a single reaction, the presence or absence of the factor II 20210 mutation. This is what is represented in Figure 4, obtained from a cell line ~~homozygous~~heterozygous for the factor II 20210 mutation. Comparable results are obtained using a clinical example.

Please replace the paragraph beginning on page 22, line 3, with the following rewritten paragraph:

Cell lines – Three ~~lymphoblast~~lymphoblastoid cell lines of known genotype for the factor V Leiden ~~mutations~~mutation and the factor II 20210 mutation (Coriell cell repository) were used:
The GM14899 line expresses only the factor V Leiden mutation: this line is homozygous for the factor V Leiden mutation (A/A) and homozygous for the wild-type allele at position ~~2012~~20210 of factor II (G/G). The GM16000C line expresses only the factor II 20210 mutation: this line is homozygous for the factor II 20210 mutation (A/A) and homozygous for the wild-type allele at position 1691 of factor V (G/G). The GM16028B line is heterozygous for the 2 mutations (G/A).

Please replace the paragraph beginning on page 22, line 27, with the following rewritten paragraph:

Cloning of the region of interest: In order to obtain a large amount of DNA of the region that may express the factor V Leiden mutation, a PCR was carried out using the genomic DNA as obtained above, from cell lines or from blood samples, using a pair of amplification primers comprising SEQ ID ~~No.~~NO: 3~~,~~ (5' AGTGCTTAACAAGACCATACTA 3') for the first

primer, and SEQ ID ~~No.~~NO: ~~4,~~ (5' AACAGACCTGGAATTTGAAACTAA 3') for the second primer. The parameters of the PCR were as follows: 2 min at 95°C; 30 cycles of 30 s at 95°C, 30 s at 55°C, 30 s at 72°C; followed by 7 min at 72°C). The amplicons thus obtained were cloned into a vector PUC19 and verified by sequencing. The plasmids, containing either a nucleotide G or a nucleotide A at position 1691, were amplified and purified using a plasmid Maxi kit (Qiagen; Germany).

Please replace the paragraph beginning on page 23, line 6, with the following rewritten paragraph:

In order to obtain a large amount of DNA of the region that may express the factor II 20210 mutation, a PCR was carried out using the genomic DNA as obtained above, from cell lines or from blood samples, using a pair of amplification primers comprising SEQ ID ~~No.~~NO: ~~7,~~ (5' TCTAGAAACAGTTGCCTGGC 3') for the first primer, and SEQ ID ~~No.~~NO: ~~8,~~ (5' CTACCAGCGTGCCACCAGGT 3') for the second primer. The parameters of the PCR were as follows: 2 min at 95°C; 30 cycles of 30 s at 95°C, 30 s at 55°C, 30 s at 72°C; followed by 7 min at 72°C. The amplicons thus obtained were cloned into a vector PCR-Trap (GeneHunter, USA) and verified by sequencing. The plasmids, containing either a nucleotide G or a nucleotide A at position 1691, were amplified and purified using a plasmid Maxi kit (Qiagen; Germany).

Please replace the paragraph beginning on page 23, line 18, with the following rewritten paragraph:

In order to determine the genotyping of the DNA taken from a patient or from a cell line, a factor V amplification reaction mixture (40 mM Tris HCl, pH 8.5; 12 mM $MgCl_2$; 100 mM KCl; 5 mM dithiothreitol; 15% v/v DMSO; 1 mM dNTP) was prepared containing the amplification primers for amplifying the region that may contain the FV Leiden mutation:

- 0.2 µM (final concentration) of a first amplification primer of SEQ ID ~~No.~~NO: ~~2,~~ (5' AGT GCT TAA CAA GAC CAT ACT A 3'),
- 0.2 µM (final concentration) of a second amplification primer of SEQ ID ~~No.~~NO: ~~1,~~ (5' AAA TTC TCA GAA TTT CTG AAA GG 3') comprising the T7 phage polymerase promoter, i.e. an amplification primer whose complete sequence

corresponds to SEQ ID ~~No.~~NO: 13~~,~~ (5' aat tct aat acg act cac tat agg gag aAA ATT CTC AGA ATT TCT GAA AGG 3'),

- 0.05 µM (final concentration) of "molecular beacons" of SEQ ID ~~No.~~NO: 9~~,~~ (5' CTG GAC AGG CGA IGA A 3'), labeled with a ROX (6-carboxy-X-rhodamine) fluorophore in the 5' position, and of a "quencher" (Dabsyl) in the 3' position (complete sequence: 5' ROX-*cgatcg* CTGGACAGGCGAIGAA*cgatcg*-Dabsyl 3' (SEQ ID NO: 20)). This "molecular beacon" made it possible to reveal the absence of the Leiden mutation,
- 0.025 µM (final concentration) of "molecular beacons" of SEQ ID ~~No.~~NO: 10~~,~~ (3' CTG GAC AGG CAA IGA A 3'), labeled with a FAM (~~6-carboxy-fluorescein~~6-carboxyfluorescein) fluorophore in the 5' position, and of a "quencher" (Dabsyl) in the 3' position (complete sequence: 5' FAM-*cgatcg* CTGGACAGGCAAIGAA*cgatcg*-Dabsyl 3' (SEQ ID NO: 21)). This "molecular beacon" made it possible to reveal the presence of the Leiden mutation.

Please replace the paragraph beginning on page 24, line 10, with the following rewritten paragraph:

In order to determine the genotyping of the DNA taken from a patient or from a cell line, a factor II amplification reaction mixture (40 mM Tris HCl, pH 8.5; 12 mM $MgCl_2$; 70 mM KCl; 5 mM dithiothreitol; 15% v/v DMSO; 1 mM dNTP) was prepared containing the amplification primers for amplifying the region that may contain the FII + 20210 mutation~~:~~.

Please replace the paragraph beginning on page 24, line 15, with the following rewritten paragraph:

For factor II, the following were added to the reaction medium:

- 0.2 µM (final concentration) of a first amplification primer of SEQ ID ~~No.~~NO: 16, (5' CTGGAACCAATCCCGTGAAAG 3'),
- 0.2 µM (final concentration) of a second amplification primer of SEQ ID ~~No.~~NO: 15~~,~~ (5' AGCTGCCCATGAATAGCACT 3'), also comprising the T7 phage polymerase promoter, i.e. corresponding to SEQ ID ~~No.~~NO: 19~~,~~ (5' aattctaatacgactcactataggAGCTGCCCATGAATAGCACT 3'),

- 0.1 µM (final concentration) of "molecular beacons" of SEQ ID ~~No.~~NO: 17~~,~~ (5' ACT CTC AGC AAG CCT CAA 3'), labeled with a ROX (6-carboxy-X-rhodamine) fluorophore in the 5' position, and of a "quencher" (Dabsyl) in the 3' position (complete sequence: 5' ROX-cga tcg ACT CTC AGC AAG CCT CAA cga tcg-Dabsyl 3' (SEQ ID NO: 24)). This "molecular beacon" made it possible to reveal the presence of the factor II 20210 mutation,
- 0.1 µM (final concentration) of "molecular beacons" of SEQ ID ~~No.~~NO: 18~~,~~ (5' TCTCAGCGGGCCTCA 3'), labeled with a FAM (6-carboxyfluorescein) fluorophore in the 5' position, and of a "quencher" (Dabsyl) in the 3' position (complete sequence: ~~5' FAM- cgteg TCTCAGCGGGCCTCA cgaeg-Dabsyl 3'~~5' FAM- cgatcg TCTCAGCGGGCCTCA cgatcg-Dabsyl 3' (SEQ ID NO: 25)). This "molecular beacon" made it possible to reveal the absence of the factor II 20210 mutation.

Please replace the paragraph beginning on page 25, line 3, with the following rewritten paragraph:

As shown in Figure 5, the "molecular beacon" of SEQ ~~No.~~NO: 9 labeled with a FAM fluorophore is very specific for the mutated allele: in fact, the fluorescence was exponential, before the appearance of a plateau, when the reaction was carried out using cell lines expressing the Leiden mutation (curves of triangles; and of crosses, Figure 5), while the fluorescence remained baseline when the reaction was carried out using a cell line not expressing the Leiden mutation (white circle curve; Figure 5).

Please replace the paragraph beginning on page 25, line 9, with the following rewritten paragraph:

The "molecular beacon" of SEQ ID ~~No.~~NO: 10, labeled with a ROX fluorophore, is specific for the wild-type allele. In fact, the fluorescence was exponential when the reaction was carried out using cell lines expressing the Leiden wild-type genotype (curve of circles and crosses; Figure 6), while the fluorescence remained baseline when the reaction was carried out using a cell line not expressing the wild-type genotype (Figure 6, curve of triangles).

Please replace the paragraph beginning on page 25, line 15, with the following rewritten paragraph:

By using 2 different fluorophores, the "molecular beacon" of SEQ ID ~~No.~~NO: 10 is used simultaneously with a "molecular beacon" of SEQ ID ~~No.~~NO: 9, which made it possible to very rapidly detect, using a single reaction, the presence and/or absence of the mutation for the two factor V gene alleles. By virtue of the analysis of Figures 5 and 6, it is therefore possible to determine whether the sample has the G/G, G/A, or A/A genotype.

Please replace the paragraph beginning on page 25, line 20, with the following rewritten paragraph:

These two "molecular beacons", used simultaneously with the amplification primers of SEQ ID ~~No.~~NO: 2 and SEQ ID ~~No.~~NO: 1, therefore make it possible to differentiate clearly between the two alleles.

Please replace the paragraph beginning on page 26, line 15, with the following rewritten paragraph:

These results demonstrate that the use of a "molecular beacon" of SEQ ID ~~No.~~NO: 9 simultaneously with NASBA amplification with a pair of amplification primers, comprising a first primer comprising SEQ ID ~~No.~~NO: 1 and a second primer comprising SEQ ID ~~No.~~NO: 2, made it possible to detect very specifically the absence of the Leiden mutation. The use of a "molecular beacon" of SEQ ID ~~No.~~NO: 10 simultaneously with NASBA amplification with a pair of amplification primers, comprising a first primer comprising SEQ ID ~~No.~~NO: 1 and a second primer comprising SEQ ID ~~No.~~NO: 2, made it possible to detect very specifically the presence of the Leiden mutation.

Please replace the paragraph beginning on page 26, line 23, with the following rewritten paragraph:

As shown in Figure 7, the "molecular beacon" of SEQ ID ~~No.~~NO: 18, labeled with a FAM fluorophore, is very specific for the wild-type allele: in fact, the fluorescence was exponential, before the appearance of a plateau, when the reaction was carried out using cell lines

expressing the factor II wild-type (curves of triangles; and of crosses, Figure 7), while the fluorescence remained baseline when the reaction was carried out using a cell line not expressing the factor II wild-type polymorphism (circle curve; Figure 7).

Please replace the paragraph beginning on page 26, line 30, with the following rewritten paragraph:

The "molecular beacon" of SEQ ID ~~No.~~NO: 17, labeled with a ROX fluorophore, is specific for the mutated allele. In fact, the fluorescence was exponential when the reaction was carried out using cell lines expressing the factor II mutation (curve of circles and crosses; Figure 6), while the fluorescence remained baseline when the reaction was carried out using a cell line not expressing the wild-type genotype (Figure 6, curve of triangles).

Please replace the paragraph beginning on page 27, line 4, with the following rewritten paragraph:

By using 2 different fluorophores, the "molecular beacon" of SEQ ID ~~No.~~NO: 17 is used simultaneously with a "molecular beacon" of SEQ ID ~~No.~~NO: 18, which made it possible to very rapidly detect, using a single reaction, the presence or absence of the mutation for the factor II gene. By virtue of the analysis of Figures 7 and 8, it is therefore possible to determine whether the sample has the G/G, G/A or A/A genotype.